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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/731,224	12/09/2003	Neil P. Desai	638772000300	4904

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EXAMINER	
TSAY, MARSHA M	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/731,224	DESAI ET AL.	
	Examiner	Art Unit	
	Marsha M. Tsay	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/07/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1,4-18,84,97,98,100-108,110-117,119-128,130-132,134-137,139-141,143-218,220,221 and 224.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 4,15-18,102,108,110-117,119-127,143-147,149-151,154-181,184-188,191-195,198-202,205,208,212-216,220,221 and 224.

Continuation of Disposition of Claims: Claims rejected are 1,5-14,84,97,98,100,101,103-107,128,130-132,134-137,139-141,148,152,153,182,183,189,190,196,197,203,204,206,207,209-211,217 and 218.

This Office action is in response to Applicants' remarks received July 7, 2009.

Applicants' arguments have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn.

Claims 2-3, 19-83, 85-96, 99, 109, 118, 129, 133, 138, 142, 219, 222-223, 225 are canceled. Claims 4, 15-18, 102, 108, 110-117, 119-127, 143-147, 149-151, 154-181, 184-188, 191-195, 198-202, 205, 208, 212-216, 220-221, 224 are withdrawn. Claims 1, 5-14, 84, 97-98, 100-101, 103-107, 128, 130-132, 134-137, 139-141, 148, 152-153, 182-183, 189-190, 196-197, 203-204, 206-207, 209-211, 217-218 are currently under examination.

Priority: The request for benefit to provisional application 60/432317, filed December 9, 2002, is acknowledged.

Objections and Rejections

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 5-14, 84, 97-98, 100-101, 103-107, 128, 130-132, 134-137, 139-141, 148, 152-153, 182-183, 189-190, 196-197, 203-204, 206-207, 209-211, 217-218 are rejected under 35 U.S.C. 103(a) as being unpatentable over Desai et al. (WO 0071079; IDS 02.23.07, previously cited) in view of Gelfand et al. (EP 0227593; IDS 12,20.04, previously cited) and further in view

of Flournoy (1991 Eur J Clin Microbiol Infect Dis 10(7): 597-598; IDS 06.13.07, previously cited).

The instant claims are essentially drawn to a pharmaceutical composition comprising human serum albumin (pharmaceutical carrier), deferoxamine, and a pharmaceutical agent (paclitaxel). The deferoxamine is present in an amount effective to inhibit microbial growth and the weight ratio of human serum albumin to pharmaceutical agent is about 1:1 to about 18:1.

Desai et al. disclose a composition comprising a water insoluble pharmacological agent (i.e., paclitaxel) and a carrier protein (i.e., human serum albumin) (p. 8 lines 9-24). Desai et al. further disclose that said composition can be sterile and can be formed into nanoparticles of less than or equal to 200 nm, and that the ratio of albumin to pharmaceutical agent can be about 13:1 (p. 8 lines 25-28, p. 46 example 6). Desai et al. also disclose that the nanoparticles may be lyophilized and may be resuspended in an aqueous solution to the original dispersion (p. 46 example 6). Desai et al. disclose that the paclitaxel is free of cremophor (p. 8 lines 13-14). Desai et al. further disclose that said compositions can comprise antimicrobials as the pharmaceutical agent (p. 28), as well as suggest that more than one pharmacological agent(s) can be combined together to form said composition (p. 108 lines 5-8). Desai et al. also disclose using said compositions for reducing neurotoxicity of a pharmacological active agent, i.e. paclitaxel (p. 36 lines 4-6). Desai et al. do not explicitly teach that said composition comprises both paclitaxel and an antimicrobial agent.

Gelfand et al. disclose that iron chelating agents, particularly deferoxamine, in connection with the synergistic treatment of cancer, can be prepared in combination with cancer drugs, including vinblastine (an antimicrotubule agent) (abstract and p. 3 line 38). Gelfand et al. also

disclose that the use of iron chelating agents in combination with cytostatic agents can mitigate toxic side effects caused by cytostatics (p. 2 lines 44-45). Gelfand et al. do not teach deferoxamine has antimicrobial properties.

Flournoy discloses that deferoxamine mesylate (DFM) is an iron chelator with antimicrobial properties (p. 597).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Desai et al. by further incorporating the deferoxamine of Gelfand et al. and Fluornoy into the human serum albumin:paclitaxel composition of Desai et al. (claims 1, 5-14, 84, 97-98, 100-101, 103-107, 128, 130-132, 134-137, 139-141, 148, 152-153, 182-183, 189-190, 196-197, 203-204, 206-207, 209-211, 217-218). The motivation to do so is given by Desai et al., which suggest that pharmacological active agents (i.e. antineoplastics, antimicrobials) can be combined into a composition with an albumin protein carrier and Gelfand et al. and Fluornoy et al., which disclose that deferoxamine is an iron chelator that has a synergistic effect when used with antineoplastic drugs (i.e. antimicrotubule agents), such that said effect can mitigate the toxic effects of said drugs, as well as having antimicrobial properties. Therefore, it would be reasonable for one of ordinary skill to recognize that it would be beneficial in inhibiting the toxic effects of a cytostatic agent as well as the growth of microorganisms in said composition. Regarding the effective amount of deferoxamine, it would have been a matter of routine experimentation for one of ordinary skill to administer said deferoxamine at a dosage that would not cause a toxicological effect in a patient.

In their remarks, Applicants assert that (1) there is no motivation to modify the teachings of Desai et al. by further incorporating the deferoxamine of Gelfand et al. and Flournoy et al. into the human serum albumin:paclitaxel composition. Desai et al. do not teach a composition which comprises both paclitaxel and an antimicrobial agent. Desai et al. provide a list of substantially water insoluble pharmacologically active agents, such as antineoplastics and antimicrobials, which can be used as the pharmaceutical active agent (p. 24 line 10 to page 30 line 25). Desai et al. do not teach or suggest the use of an antimicrobial agent (i.e. deferoxamine) to inhibit microbial growth in a pharmaceutical composition. (2) There is no teaching or suggestion in Gelfand et al. to combine paclitaxel with deferoxamine. Paclitaxel is not even mentioned in the disclosure of Gelfand et al. Further, Gelfand et al. teach the use of iron chelating agents, particularly deferoxamine, in connection with synergistic treatment of cancer with cytostatically effective preparations. No taxane, much less placlitaxel, was even tested in Gelfand et al. A person in the art would have no motivation to combine Gelfand et al. with Desai et al. to achieve the claimed and elected pharmaceutical compositions. (3) Flournoy does not cure the deficiencies of either Desai et al. or Gelfand et al. Flournoy is cited as teaching that deferoxamine mesylate has antimicrobial properties. Flournoy does not teach or suggest a pharmaceutical composition comprising both deferxamine mesylate and an active agent such as paclitaxel. Applicant's arguments have been fully considered but they are not persuasive.

(1) Reply: Desai et al. disclose that pharmacological agent(s) can be present in a broad range of concentration in the invention composition as determined by the end use application of said invention composition (p. 31 lines 1-5). Further, throughout pages 36-42, Desai et al. further disclose that the pharmacological agents disclosed (on pages 24-30) can be used in

combination with other suitable pharmacological active agent(s). Desai et al. also disclose using said compositions for reducing neurotoxicity of a pharmacological active agent, i.e. paclitaxel (p. 36 lines 4-6). Therefore, it would be reasonable for one of ordinary skill to know that the Desai et al. reference at least discloses the combination of pharmacological agent(s). The deficiency of Desai et al. to not explicitly teach that said composition comprises both paclitaxel and an antimicrobial agent is believed to be remedied by Gelfand et al.

(2) Reply: Gelfand et al. disclose that cytostatic agents can be combined with deferoxamine in order to mitigate toxic side effects which are caused by cytostatic agents (p. 2 lines 44-45). Gelfand et al. disclose examples of cytostatic agents to include vinblastine (an antimicrotubule agent) (p. 2 line 38). It is known in the art that paclitaxel is a cytostatic agent and also an antimicrotubule agent. Therefore, it would be reasonable for one of ordinary skill to combine the paclitaxel of Desai et al. with the deferoxamine of Gelfand et al. because Gelfand et al. suggest the combination of deferoxamine with a cytostatic agent from the same class of cancer drugs.

(3) Reply: The Flournoy reference is cited for further evidence to show that deferoxamine has antimicrobial properties in addition to mitigating toxic side effects caused by cytostatics.

For at least these reasons, the 103(a) rejection is maintained.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is (571)272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR

system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Maryam Monshipouri/

Primary Examiner, Art Unit 1656

November 4, 2009

Marsha Tsay
Art Unit 1656